PROGRAM PROJECTS ON AUTOIMMUNITY

NIH GUIDE, Volume 22, Number 21, June 11, 1993

RFA: AI-93-018

P.T. 34; K.W. 0715015, 0755030, 0765033, 0411005, 0745027

National Institute of Allergy and Infectious Diseases
National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: August 15, 1993
Application Receipt Date: November 16, 1993

PURPOSE

The Division of Allergy, Immunology and Transplantation of the National Institute of Allergy and Infectious Diseases (NIAID) and the Rheumatic Diseases Branch of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invite studies aimed at elucidating the causes and mechanisms of tolerance and autoimmune diseases and at the application of this basic biomedical knowledge to the development and implementation of new preventive and treatment modalities for these diseases. This Request for Applications (RFA) invites applications from collaborating basic science and clinical research investigators who are interested in developing novel integrated studies on autoimmune diseases.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Program Projects on Autoimmunity, is related to the priority areas of diabetes and chronic disabling diseases, and immunization and infectious diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the

Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-782-3238).

ELIGIBILITY REQUIREMENTS

Research grant applications may be submitted by domestic, for-profit and non-profit organizations, public and private institutions, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign organizations are not eligible to apply. Applications from minority individuals and women are encouraged.

MECHANISM OF SUPPORT

The mechanism of support will be the Program Project (P01) grant. Multidisciplinary approaches that involve collaborative efforts among investigators in the fields of basic immunology, molecular biology, cell biology, biochemistry, genetics, and relevant medical specialties are strongly encouraged.

The total project period for applications submitted in response to this RFA may not exceed five years. At this time, the NIAID is administratively limiting the duration of P01 grants to four years; this administrative limitation may change in the future. If, by the beginning of the last year of support, the NIAID and NIAMS have not announced intentions to readvertise the RFA, incumbents who wish to recompete may consider reapplying using the investigator-initiated Interactive Research Project Grant (IRPG) mechanism. Applicants should be alert to a program announcement concerning IRPGs published in the NIH Guide for Grants and Contracts, Volume 22, Number 16, April 23, 1993. In such instances, incumbents are strongly encouraged to contact NIAID Program Staff prior to submitting an application.

FUNDS AVAILABLE

The estimated total funds (direct and indirect costs) available for the first year of support for awards under this RFA will be $2,300,000. In Fiscal Year 1994, the NIAID and the NIAMS plan to fund approximately three program projects. Applications may not request budgets in excess of $500,000 total direct costs in the first year or more than 4 percent annual inflationary increases for future

years. An application with a first year requested amount in excess of $500,000 total direct cost will require written approval by senior NIAID or NIAMS officials via the program officer for acceptance of the application for processing. The usual PHS policies governing grants administration and management will apply. This level of support is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NIAID and the NIAMS, awards pursuant to this RFA are contingent upon the availability of funds for this purpose. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and availability of funds.

RESEARCH OBJECTIVES AND SCOPE

The major goals of these program projects are: increased understanding of etiology and pathogenetic mechanisms involved in autoimmune diseases; generation of new information and the expansion of the current knowledge base; and the application of this knowledge to the development of new or improved measures of risk assessment, prevention, early diagnosis and treatment of a wide variety of autoimmune diseases and disorders in which the autoimmune response is a major contributor to pathogenesis.

The NIAID and NIAMS are seeking innovative applications that address various aspects of the immune responses related to self reactivity, which may include studies concerned with relevant areas of genetics, cell and molecular biology, biochemistry, physiology, microbiology, pathology and pharmacology. Of special interest are program projects that emphasize new ideas, novel approaches, and state-of-the-art technology in basic research that elucidates pathogenic mechanisms and shows promise for clinical application in the prevention, diagnosis, and treatment of autoimmune diseases.

There is overwhelming evidence to implicate immune mechanisms in the pathogenesis of diseases of the skin, nervous system, endocrine system, and gastrointestinal tract. Thus, in addition to studies of well-recognized autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, antibody-mediated thrombocytopenia and autoimmune hemolytic anemia, the NIAID and NIAMS encourage investigators to design and develop studies aimed at establishing the role of the immune system in the pathogenesis of endocrine,

dermatologic, neurologic and gastrointestinal diseases and the development of new preventive and treatment modalities specific for these disorders through the manipulation of the immune response.

Projects focused on the study of mechanisms of autoimmune diseases should be designed based on integrated and coordinated intra-institutional clinical investigations or experimental studies with demonstrated relevance to human autoimmune disease. Inclusion of basic research components utilizing samples from human source materials in in vitro procedures are encouraged, as are preclinical studies using appropriate animal models of human autoimmune disease. Inclusion of clinical investigative components drawing upon immunologically relevant areas in medicine, pediatrics, surgery, dermatology, neurology, pathology and their subspecialties is highly recommended.

Preparation of the Application

In preparing the application, the applicant should bear in mind the research objectives of this RFA. P01 applications should be prepared using the guidance and instructions provided in the NIAID Information Brochure for Program Project and Center Grants, which may be requested from Dr. Rohrbaugh at the address listed under INQUIRIES. Failure to follow these instructions may result in delays in the review or in an incomplete application.

STUDY POPULATIONS

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy requires that applicants for NIH clinical research grants and cooperative agreements include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or

inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale MUST be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in items 1-4 of the Research Plan AND summarized in item 5, Human Subjects.

Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations [i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics]. The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, clinical samples which may be coded for use by the applicant but could be identified by another source are not excluded. Every effort should be made and documented to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For studies in foreign populations, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the U.S. populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

LETTER OF INTENT

Prospective applicants are asked to submit, by August 15, 1993, a letter of intent that includes a descriptive title of the overall proposed research, the name, address and telephone number of the Program Director, the number and title of this RFA, and a list of the key investigators and their institution(s). Although the letter of intent is not required, is not binding, does not commit the sender to submit an application, and does not enter into the review of subsequent applications, the information that it contains allows NIAID and NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review. The letter of intent is to be sent to Dr. Mark Rohrbaugh at the address listed under INQUIRIES.

APPLICATION PROCEDURES

Applications are to be submitted on the standard research grant application form PHS 398 (rev. 9/91). For purposes of identification and processing, item 2a on the face page of the application must be marked "YES" and the RFA number and the words "PROGRAM PROJECTS ON AUTOIMMUNITY" must be typed in.

These application forms may be obtained from the institution's office for sponsored research or its equivalent, and from the Office of Grants Inquiries,

Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20892, telephone (301) 594-7248.

It is highly recommended that the Chief of the Clinical Immunology Branch, NIAID Division of Allergy, Immunology and Transplantation, or the Chief of the NIAMS Rheumatic Diseases Branch be contacted in the early stages of preparation of the application. (See program contacts in INQUIRIES, below.)

Applications must be received by November 16, 1993.

Applications that are not received by November 16, 1993, or that do not conform to the instructions contained in PHS 398 (rev. 9/91) application kit, will be judged non-responsive and will be returned to the applicant.

The RFA label available in the application form PHS 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

Submit a signed, typewritten original of the application, including the checklist, and three signed, exact, single-sided photocopies, in one package to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

At the time of submission, two additional exact copies of the grant application and all five sets of appendix material must also be sent to Dr. Mark Rohrbaugh at the address listed under INQUIRIES.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator could be included with the application.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by the NIH Division of Research Grants (DRG) and for responsiveness by NIAID and NIAMS staff; those judged to be incomplete or non-responsive will be returned without review.

Those applications that are complete and responsive may be subjected to a triage by a peer review group to determine their scientific merit relative to other applications received in response to this RFA. The NIAID and the NIAMS will withdraw from competition those applications judged to be non-competitive for award and will notify the applicant and institutional business officials.

Those applications judged by the reviewers to be competitive for award will be further reviewed for scientific and technical merit by a review committee convened by the Division of Extramural Activities, NIAID. The second level of review will be provided by the National Advisory Allergy and Infectious Diseases Council and/or the National Arthritis and Musculoskeletal and Skin Diseases Council.

The factors to be considered in the evaluation of scientific merit of each application will be those used in the review of traditional research project grant applications, including: the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; and the adequacy and suitability of the facilities. Additional review criteria used for program project applications are outlined in the NIAID Information Brochure on Program Project and Center Grants. While the following review factors do not usually influence the priority score, they are nonetheless carefully considered by the initial review group: the appropriateness of the requested budget to the work proposed; the adequacy of protection of human subjects and/or animals in research; and the adherence, whenever appropriate, to NIH guidelines concerning adequate representation of women and minorities in clinical research. Any documented concerns expressed by the initial review group about any of these factors on a given application may influence the recommendation of the Advisory Council concerning funding of that application.

AWARD CRITERIA

Funding decisions will be made on the basis of scientific and technical merit as determined by peer review, program needs and balance, and the availability of funds.

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.
The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Howard B. Dickler, M.D.
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
Solar Building, Room 4A19
Bethesda, MD 20892
Telephone: (301) 496-7104
FAX: (301) 402-2571

Susana A. Serrate-Sztein, M.D.
Rheumatic Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 405
Bethesda, MD 20892
Telephone: (301) 594-9953
FAX: (301) 594-9673

Direct inquiries regarding review issues (including the preparation of a program project application), address the letter of intent to, and mail two copies of the application and all five sets of appendices to:

Mark Rohrbaugh, Ph.D.
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Solar Building, Room 4C22
6003 Executive Boulevard

Bethesda, MD 20892
Telephone: (301) 496-8424
FAX: (301) 402-2638

Direct inquiries regarding fiscal matters to:

Mr. Jeffrey Carow
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Solar Building, Room 4B29
6003 Executive Boulevard
Bethesda, MD 20892
Telephone: (301) 496-7075

Schedule

Letter of Intent Receipt Date: August 15, 1993
Application Receipt Date: November 16, 1993
Scientific Review Date: February 1994
Advisory Council Date: June 1994
Earliest Award Date: August 1994

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance, No. 93.855 - Immunology, Allergy and Transplantation Research and No. 93.846 - Arthritis and Musculoskeletal and Skin Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.